Neuromuscular Junction "Motor end plate"

Motor end plate "Neuromuscular Junction"

Neuromuscular transmission and Myasthenia Gravis

By

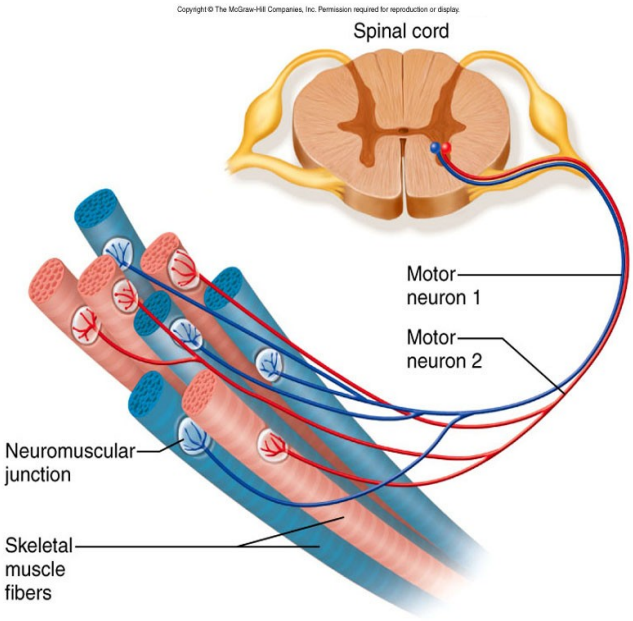
Ass. Prof. Mona Gamal El Din Al Anan

ILOs: ISA, By the end of this lecture the student should be able to:

1. Describe the physiological anatomy of the neuromuscular junction.
2. Explain the mechanism of neuromuscular transmission.
3. Describe the properties of neuromuscular transmission.
4. Explain the pathophysiology of Myasthenia gravis.

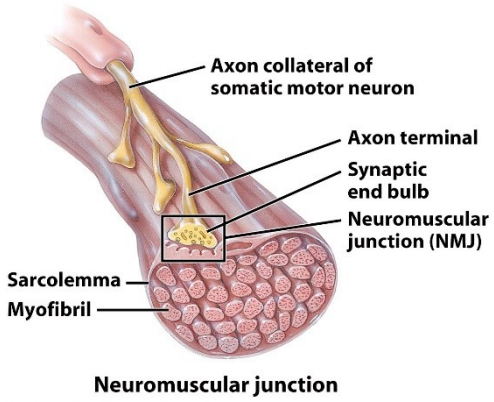
Physiologic anatomy of the neuro-muscular junction:

- Skeletal muscles are innervated by large myelinated nerve fibers, originating from the large motor neurons of the anterior horn cell of the spinal cord.
- Each nerve fiber branches many times to stimulate several skeletal muscle fibers.



Neuromuscular Junction "Motor end plate"

- The site of junction between nerve and skeletal muscle fibers is called neuromuscular junction (motor end plate), which is mostly at the fibers midpoint, so that the action potential travels in both directions.



- The nerve fiber branches at its end to form nerve terminals called *the end plate*, which invaginates into the muscle fiber, but it lies outside the cell membrane *(No cytoplasmic continuity between the nerve terminals and muscle fibers).*
- The space between the nerve terminals and muscle is called synaptic cleft and it contains cholinesterase enzyme.
- There are many mitochondria in the axon terminals that supply energy mainly for synthesis of an excitatory transmitter, *acetyl choline,* in the cytoplasm of the nerve terminals and rapidly absorbed into many synaptic vesicles.

Mechanism of neuro-muscular transmission:

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- Upon the arrival of an action potential at the axon terminal, voltage dependent calcium channels open and Ca^{++} ions flow from the extracellular fluid into the membrane of the nerve terminals.
- This Ca^{++} influx causes neurotransmitter-containing vesicles to attach to the membrane of nerve fiber.
- Fusion of the vesicular membrane with the nerve cell membrane results in the emptying of the vesicle's contents; acetylcholine, into the synaptic cleft, a process known as exocytosis.
- Acetylcholine diffuses into the synaptic cleft and binds to the acetylcholine receptors at the motor end plate.
- These receptors are ligand-gated ion channels, and when they bind acetylcholine, they open, allowing rapid influx of Na++ ions to the interior of the muscle fiber, to excite the generation of an action potential.

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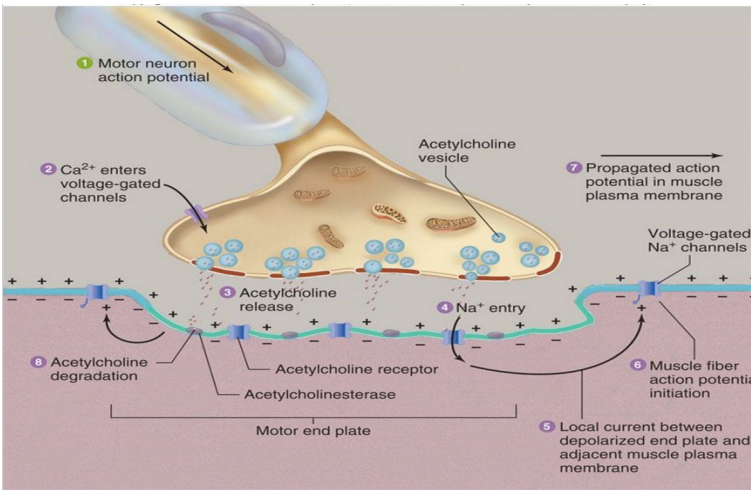

End plate potential (EPP)

- Sudden entry of sodium ions into the muscle fiber decrease the membrane potential in the local area of the end plate, creating a local potential called the end plate potential (partial depolarization of the membrane).
- The end plate potential is a local unpropagated potential when it reaches a certain value called threshold potential it fires the potential on both sides of the motor end plate, along the sarcolemmal membrane, leading to muscular contraction

Fate of acetylcholine (ACh)

- Acetylcholine is rapidly destroyed (after one millisecond) from its release, by the acetyl cholinesterase enzyme in the cleft itself.
- This short time is sufficient for acetylcholine to excite the muscle fibers.

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- The rapid hydrolysis of acetylcholine prevents re-excitation of the muscle fiber after recovery from the previous action potential.

Properties of neuromuscular transmission:

1. Unidirectional

Neuromuscular transmission occurs in one direction from the nerve to the muscle and not in the opposite direction.

2. Delay

There is some delay about 0.5 msec. in neuromuscular transmission

This time is used for release of acetylcholine, its passage across the synaptic cleft, its binding to the receptors at the outer surface of the membrane, depolarization occurs and E.P.P. is created till it reaches the firing level and an action potential is generated at the muscle fiber membrane.

3. Fatigue

The neuromuscular junction is the first site in the neuromuscular system which suffer from fatigue.

4. Can be stimulated or inhibited

Transmission of impulses at the MEP can be affected by certain drugs or diseases.

Chemical agents and diseases that affect neuromuscular junction

	Chemical agent or disease	Mechanism (block receptors at MEP)

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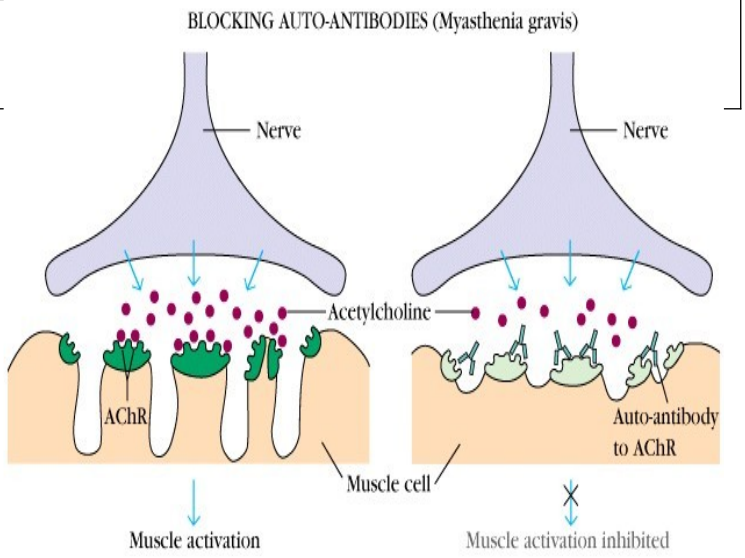
	Curare	Reversibly binds with acetylcholine receptors. Consequently paralysis ensues
	Myasthenia gravis	Self-produced antibodies inactivate acetylcholine receptor sites resulting in extreme muscular weakness
	Neostigmine	Temporarily inhibit acetylcholinesterase Is the treatment of choice in myasthenia gravis
	organophosphates	Irreversibly inhibit acetylcholinesterase Used in pesticides and military gases (toxic)
	Clostridium botulinum toxin	Block release of acetylcholine



Myasthenia gravis:

- Myasthenia gravis is a

serious disease caused by a failure of transmission at the neuromuscular junction.

- An autoimmune disease in which some of the acetyl choline receptors are destroyed by circulating antibodies
- Acetylcholine released by the impulses cann’t produce an immediate effect and is destroyed by Acetyl cholinesterase.
- Drugs which inhibit the action of acetylcholine esterase and allow accumulation of adequate amounts of acetyl choline to stimulate the remaining receptors can be used e.g. neostigmine